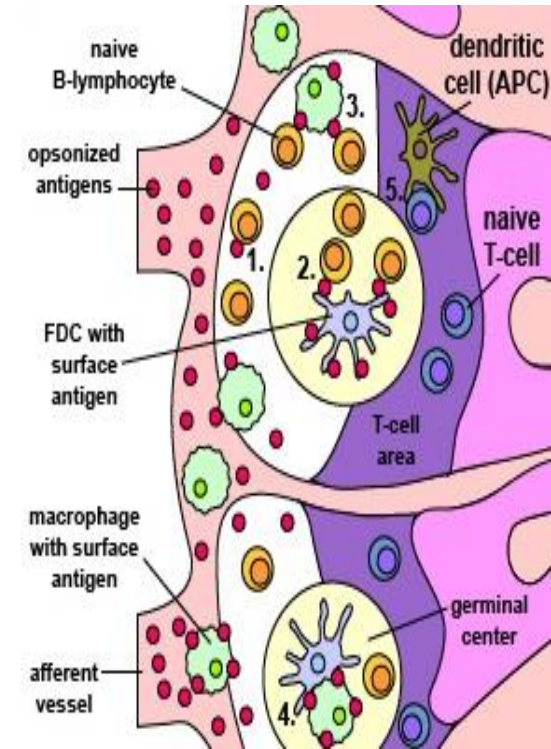
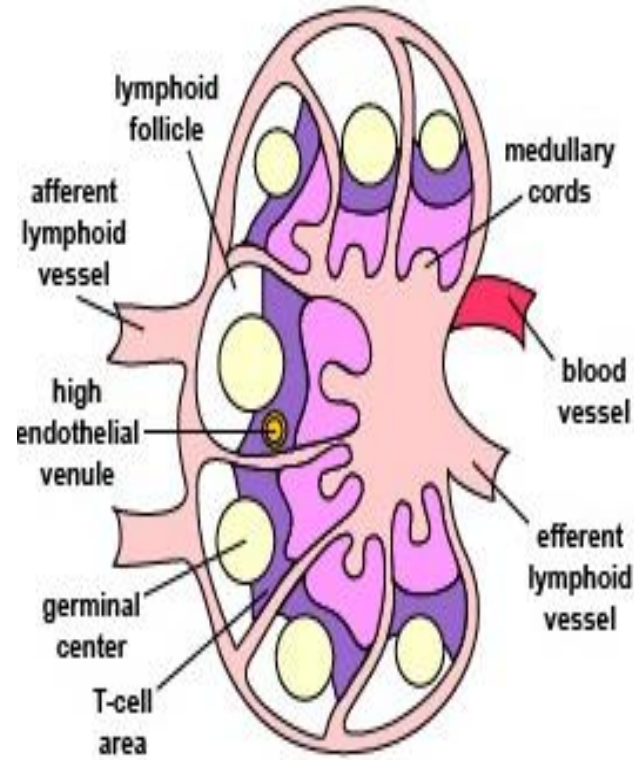


# Primary and Secondary lymphoid organs

By : Dr. AGHARID ALI HUSSEIN  
COLLEGE OF VETERINARY MEDICINE  
/TIKRIT UNIVERSITY /THIRD LEVEL



**THIS LECTURE DEALS WITH:**

- TYPE OF ORGANS IN THE IMMUNE SYSTEM**
- ROLE OF PRIMARY AND SECONDARY LYMPHOID ORGANS IN IMMUNITY**

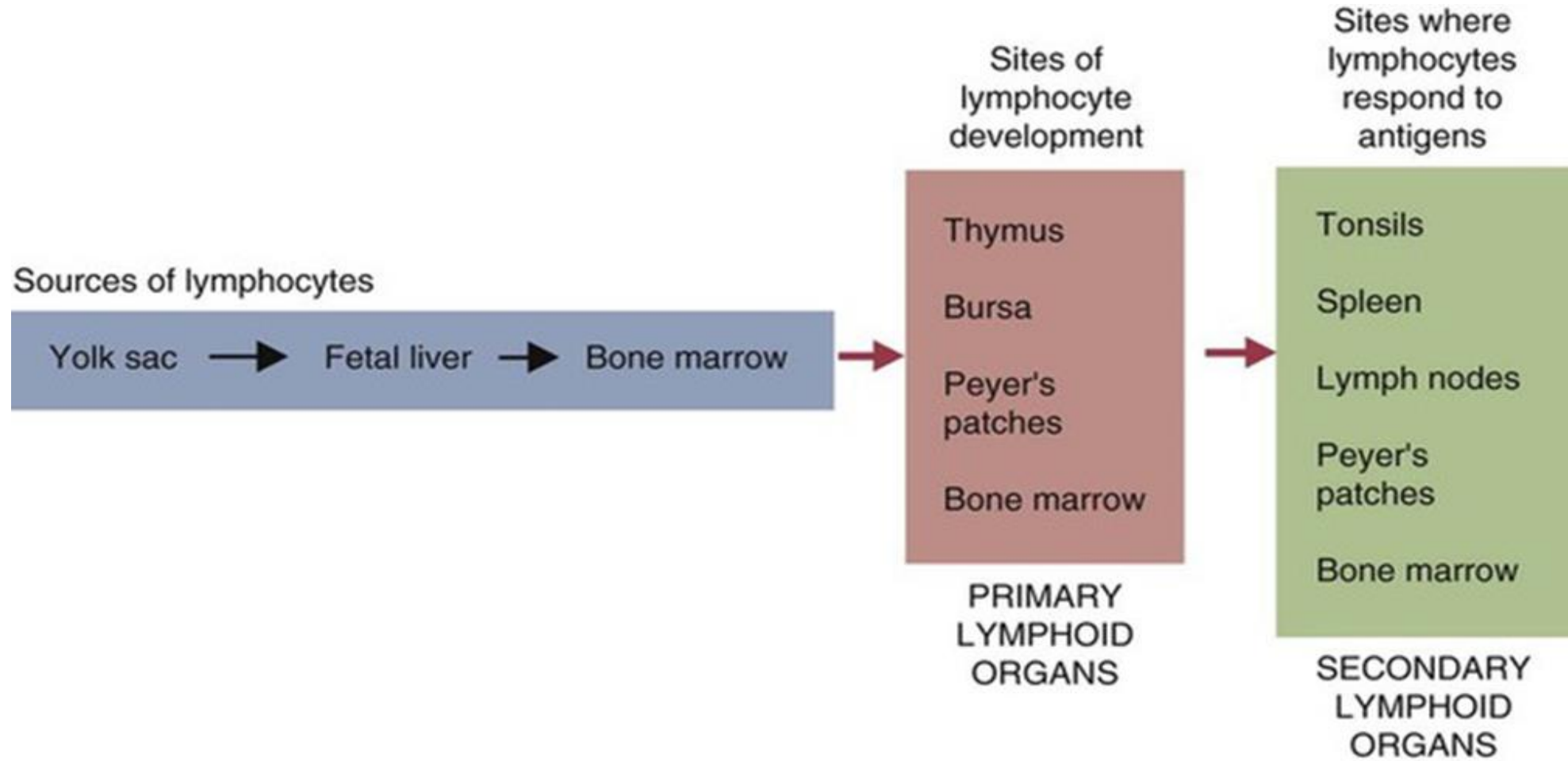
# **ORGANS OF THE IMMUNE SYSTEM**

- 1. Lymphoid organs are the important organs of the immune system.**
- 2. Lymphocytes are the highly active cells and large number of them recirculating as individual cells in blood, lymph and tissue fluids.**
- 3. Lymphocytes are the predominant cells in lymphoid organs such as the spleen, lymph nodes, and thymus (Fig. 1). environment for efficient interaction among lymphocytes, antigen-presenting cells, and foreign antigens, as well as sites where lymphocytes can respond optimally to processed antigen**

**Lymphoid organs can be classified into two groups:**

**Primary lymphoid organs**

**Secondary lymphoid organs**



**Figure 1: The lymphoid organs can conveniently be divided into three groups based on their role in the development and functioning of lymphocyte populations.**

# Primary lymphoid organs

1. Primary lymphoid organs are also called generative organs or central lymphoid organs.
2. In primary lymphoid organ, lymphocytes first express antigenic receptors and mature both phenotypically and functionally without any antigenic stimulation.
3. Mature lymphocytes fall into two major populations, T cells and B cells depending on at which primary organ they were matured.
4. T cells mature in thymus where as B cells in Bursa of Fabricius (in birds) or bone marrow (primates and rodents) or Peyer's patches (in ruminants ).
5. Examples of primary lymphoid organs: bone marrow, thymus, Bursa of Fabricius, some Peyer's patches and fetal liver.

## Secondary lymphoid organs

- ❑ They are also called peripheral lymphoid organs.
- ❑ In these organs antigens are trapped and immune response is generated based on foreign antigenic stimulation.
- ❑ These organs are rich in macrophages and dendritic cells (which trap and process antigen) and also T and B cells (which mediate immune response).
- ❑ Examples of secondary lymphoid organs: Tonsil, spleen, lymph nodes, mucosal associated lymphoid tissues (MALT), gut associated lymphoid tissues (GALT)

# PRIMARY LYMPHOID ORGANS

## 1. THYMUS

- ❑ Thymus is the first lymphoid organ to develop in mammals.
- ❑ The thymus is located in the upper front part of the chest, in the anterior [superior mediastinum](#), behind the [sternum](#), and in front of the [heart](#). It is made up of two lobes, each consisting of a central medulla and an outer cortex, surrounded by a capsule.
- ❑ In horse, cattle, sheep, and chickens, it extends up to the neck as far as to the thyroid gland.
- ❑ The size of thymus increases progressively during fetal and neonatal life and reaches maximum size during puberty (sexual maturity) after that it atrophies (Atrophy is the progressive degeneration or shrinkage of muscle or nerve tissue) but fragments persist in old age.

## Structure and Function

1. It is a bilobed lympho- epithelial organ.
  2. Each lobe consists of lobules of loosely packed epithelial cells and covered by a connective tissue capsule.
  3. The outer part of each lobule is cortex and inner part is called medulla.
- A. Cortex: It is composed of numerous lymphocytes (called thymocytes) of various stages of development, many epithelial cells and a few macrophages. Yolk sac, Bone marrow or foetal liver derived immature T (thymus dependent) cell lineage enter the thymic cortex through the blood vessels. The capillaries that supply thymic cortex are surrounded by an abnormally thick basement membrane and a continuous layer of epithelial cells, which prevent antigen from entering thymic cortex.
- B. Maturation begins in the cortex and as the immature thymocytes migrate towards medulla where they undergo positive and negative selection of thymocytes. Because of the positive and negative selection of thymocytes, 90-95% thymocytes die in the thymus by process of apoptosis and only 5-10% of thymocytes mature as mainly either CD4 + or CD8 + T-cells. Thymic epithelial cells secrete hormones like thymopoietins, thymosins, thymulin, and thymostimulins.
- Under the influence of these hormones the cells mature, thus the medulla contains mostly mature T cells. Only mature T cells from medulla exit the thymus through efferent vessels into blood circulation and peripheral lymphoid tissues, Fig.1

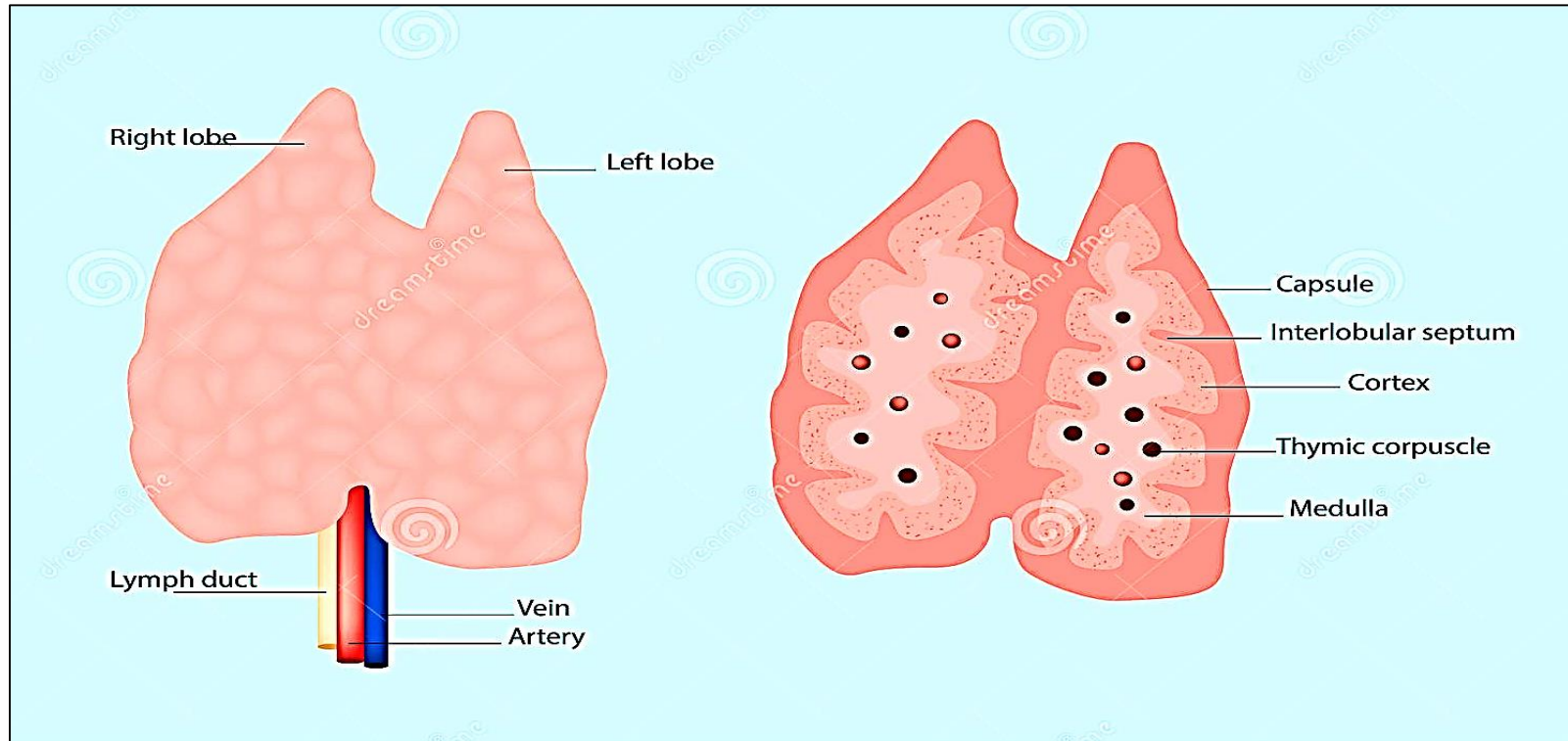


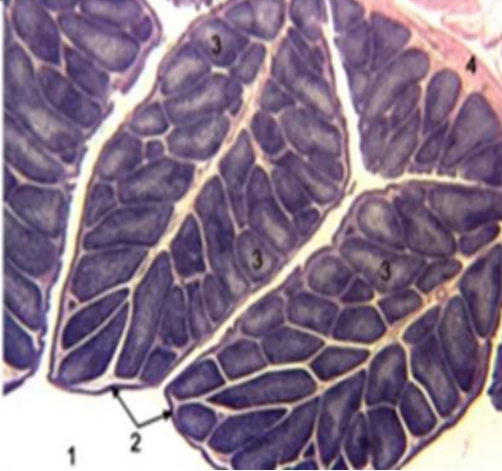
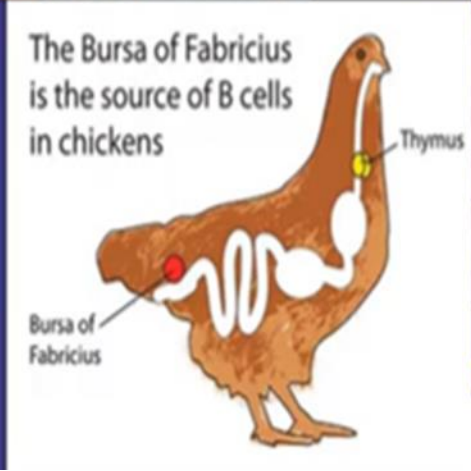
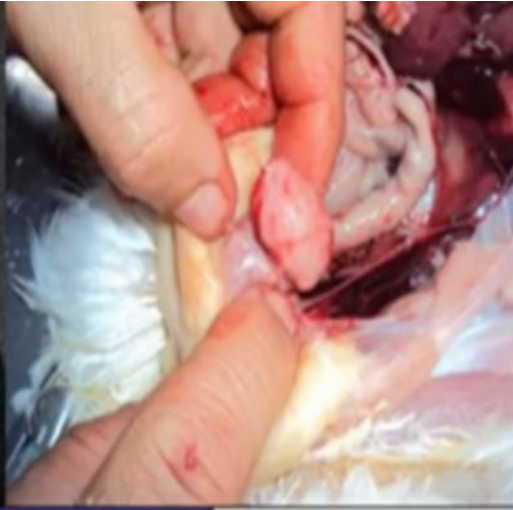
Figure 1 structure of the thymus

## **2. BURSA OF FABRICIUS**

- The bursa of Fabricius is found only in birds. It is a round sac located just above the cloaca Like the thymus, the bursa reaches its greatest size in the chick about 1 to 2 weeks after hatching and then shrinks as the bird ages. It is very difficult to identify in older birds.**
- Thus the bursa is a primary lymphoid organ that functions as a maturation and differentiation site for the cells of the antibody forming system called B cells.**
- The bursa acts like the thymus insofar as immature cells produced in the bone marrow migrate to the bursa. These cells then proliferate rapidly, but 90% to 95% of these eventually die by apoptosis; the negative selection of self-reactive B cells.**
- Once their maturation is completed, the surviving B cells emigrate to secondary lymphoid organs.**

## Structure

- ❑ Bursa consists of lymphocytes embedded in epithelial tissue. This epithelial tissue lines a hollow sac connected to the cloaca by a duct.
- ❑ Inside the sac, folds of epithelium (plicae) extend into the lumen. Each plicae contains many lymphoid follicles (bursal follicle). حويصلات
- ❑ Each follicle is divided into a cortex and medulla. The cortex is the outer part packed with lymphocytes, plasma cells and macrophages.
- ❑ The inner part is medulla. These stem cells under the influence of bursal micro environment (hormonal influence of bursepoietin/ bursin ) mature and differentiate into bursal lymphocytes or B cells.
- ❑ Differentiation of immature B- cells into immunocompetent B- cells (antibody producing cells).



## PEYER'S PATCHES

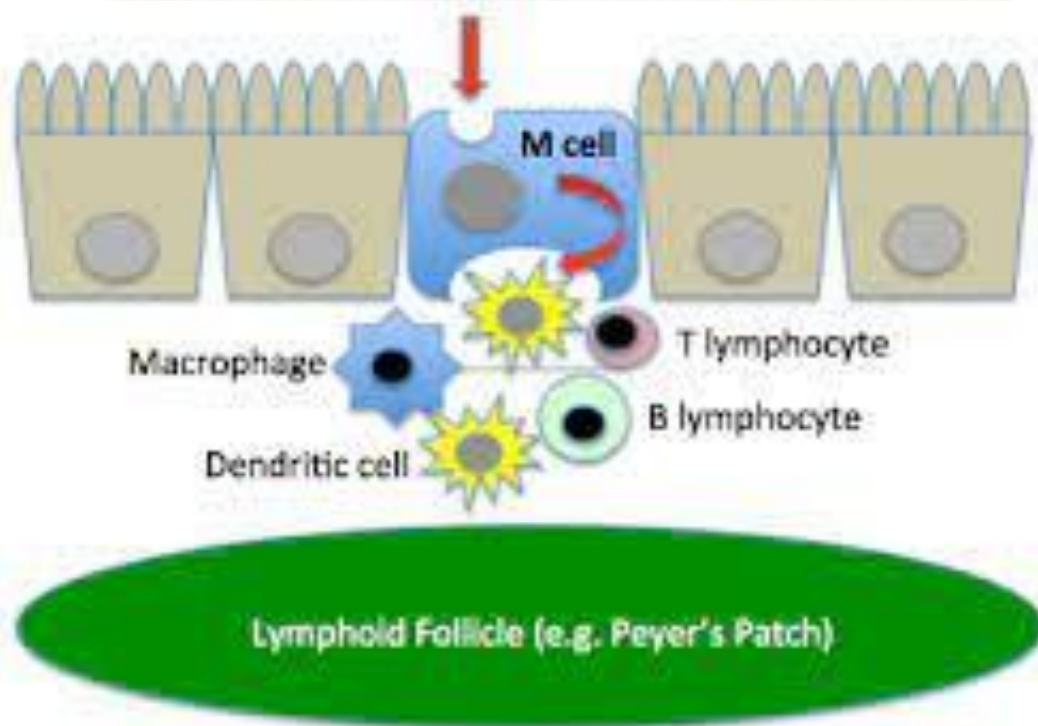
Peyer's patches (PPs) are lymphoid organs located in the walls of the small intestine. Their structure and functions vary among species. Peyer's patches thus act for the gastrointestinal system much as the tonsils act for the respiratory system, trapping foreign particles, surveilling them, and destroying them. There are M cells or microfold cells, a name given due to their unique structure. **M cells are specialized epithelial cells of the mucosa-associated lymphoid tissues including Peyer's patches (PPs)** . A characteristic of M cells is that they transport antigens from the lumen to cells of the immune system, thereby initiating an immune response or tolerance. There are two types of PP: ileal PPs and jejunal PPs

### 1. **ILEAL PPS**

- i. Ileal PPs consist of densely full lymphoid follicles each separated by a connective tissue sheath, and contain only B cells.
- ii. in ruminants, horses, dogs, and humans (group I), 80% to 90% of the PPs are found in the ileum, The ileal PPs of some group I species such as sheep function in a manner similar to the avian bursa. Thus, ileal PPs are sites of rapid B cell proliferation
- iii. **The bone marrow of lambs contains many fewer lymphocytes than the bone marrow of laboratory rodents, and the ileal PPs are therefore their most significant source of B cells.**
- iv. **The ileal PPs reach maximal size and maturity before birth and they disappear by 15 months of age and cannot be detected in adult sheep.**

**2. Jejunal PPs;** In other mammals, such as primates (, rabbits, and rodents (group II), PPs are located at random intervals in the ileum and jejunum. In these mammals, the PPs do not develop until 2 to 4 weeks after birth and persist into old age.

Bacteria, Viruses, Parasites, Proteins in Intestinal Lumen



Lymphoid Follicle (e.g. Peyer's Patch)

## Bone Marrow

- The specialized ileal PP is the primary lymphoid organ for B cells only in group I mammals such as ruminants.
- In group II mammals the bone marrow probably serves this function.
- There is no exclusive B cell development site in the bone marrow, although it is suggested that precursor B cells develop at the outer edge of the marrow and migrate to the center as they mature and multiply.
- Negative selection occurs within the bone marrow so that, as in other primary lymphoid organs, most pre-B cells generated are destroyed.

## SECONDARY LYMPHOID ORGANS

- ❑ In adult animals, most cell types reside in stable tissues and do not move a lot, in contrast, the many different cells of the immune system are highly mobile.
- ❑ Cells move from the bone marrow to the thymus and secondary lymphoid organs.
- ❑ Cells migrate around the body looking for invaders and also move from lymphoid organs to sites of microbial invasion.

In contrast to the primary lymphoid organs, the secondary lymphoid organs arise late in fetal life and persist in adults.

1. Unlike primary lymphoid organs, they enlarge in response to antigenic stimulation.
2. Surgical removal of one of them does not significantly reduce immune capability. Examples of secondary lymphoid organs include the spleen, the lymph nodes, the tonsils, and other lymphoid tissues in the intestinal, respiratory, and urogenital tracts.
3. These organs contain dendritic cells that trap and process antigens and lymphocytes that mediate the immune responses including T cells (CD8 + and CD4+) and B cells.
4. Secondary lymphoid organs are connected to both the blood and lymphoid systems, thus allowing them to continuously sample and concentrate circulating antigens.

# LYMPH NODES

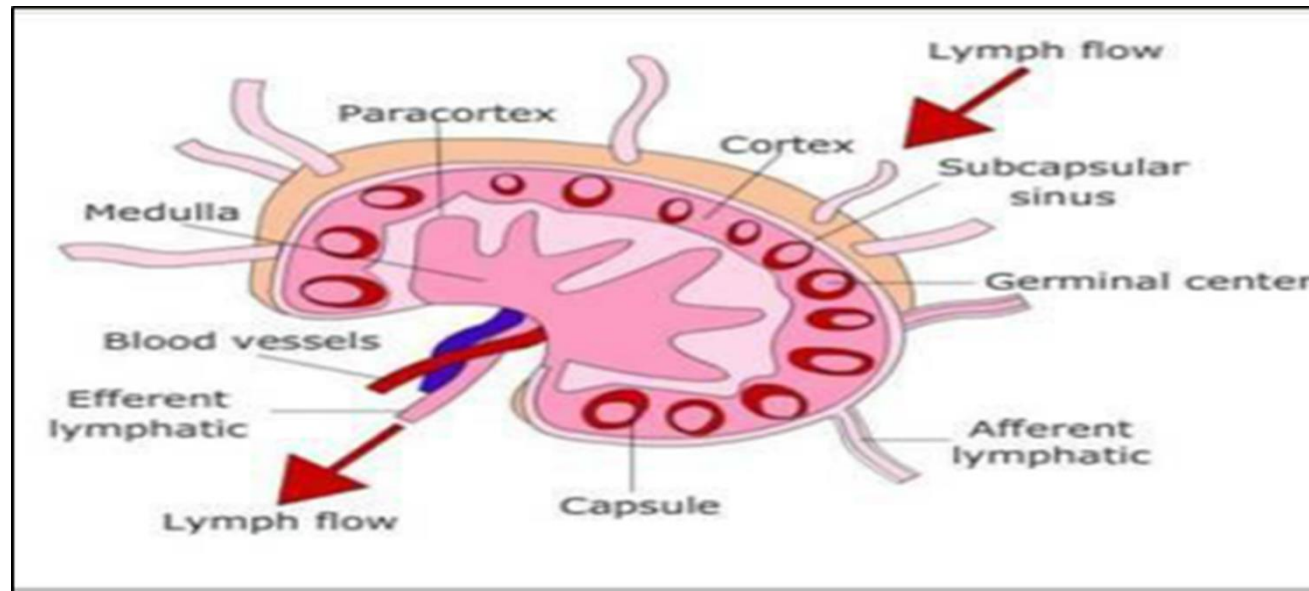
Lymph nodes are round or bean-shaped filters strategically placed on lymphatic vessels in such a way that they can sample antigens carried in the lymph

- ❑ Lymph nodes consist of a capsule beneath which is a reticular network filled with lymphocytes, macrophages, and dendritic cells, and through which lymphatic sinuses penetrate.
- ❑ The lymph node thus acts as a filter for lymph fluid.
- ❑ The interior of lymph nodes is divided into three regions: a peripheral cortex, a central medulla, and an ill-defined region in between, called the paracortex.
- ❑ B cells predominate in the cortex, where they are arranged in aggregates called follicles.
- ❑ Lymph nodes are very busy places with cells coming and going in response to a multitude of chemical signals.

## FUNCTION:

The principle function of secondary lymphoid organs such as lymph nodes is to **facilitate the interactions between antigen presenting cells (APCs) (macrophage, dendritic cells and B cells)** and **antigen-sensitive T**, each cell must be guided to its fitting contacts with great accuracy and A complex mixture of chemokines directs these cells.

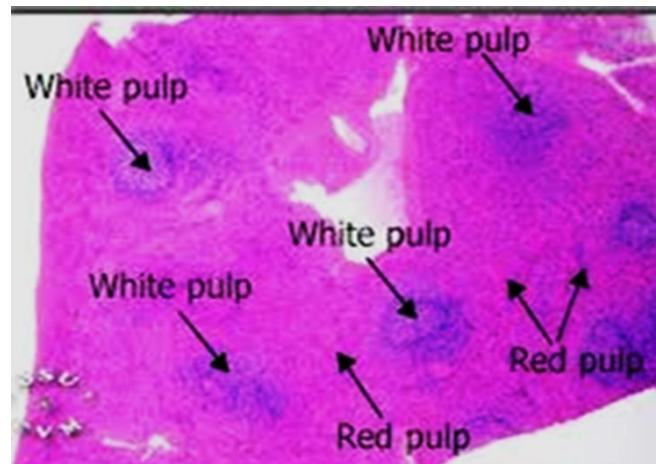
- ❑ Activate T cells ultimately exit lymph node and enter the circulation
- ❑ Activate B cells migrate into germinal center or medulla and secrete antibodies.



# Spleen

**Spleen** Just as lymph nodes filter antigens from lymph, so the spleen filters blood-borne pathogens and antigens, cellular debris, and aged blood cells.

- ❑ The spleen also stores red cells and platelets, recycles iron, and undertakes red cell production in the fetus.
- ❑ the spleen consists of two forms of tissue:
- ❑ Red pulp is used for blood filtering and for red cell storage. It contains large numbers of antigen-presenting cells, lymphocytes, and plasma cells.
- ❑ The other tissue is called the white pulp which rich in both B and T cells where immune responses occur.
- ❑ The white pulp is separated from the red pulp by a region called the marginal zone. This zone contains numerous macrophages and dendritic cells as well as a large population of B cells.



## OTHER SECONDARY LYMPHOID ORGANS:

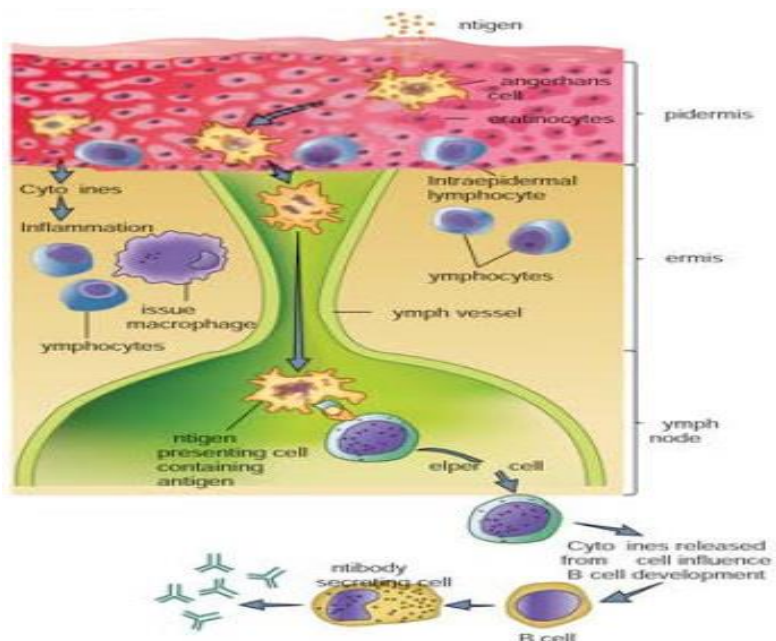
Secondary lymphoid organs include not only the spleen and lymph nodes but also the bone marrow, tonsils, and lymphoid tissues scattered throughout the body including : The mucosa-associated [lymphoid tissues](#)( MALT)and the skin-associated lymphoid tissues(SALT).

- **Bone Marrow**

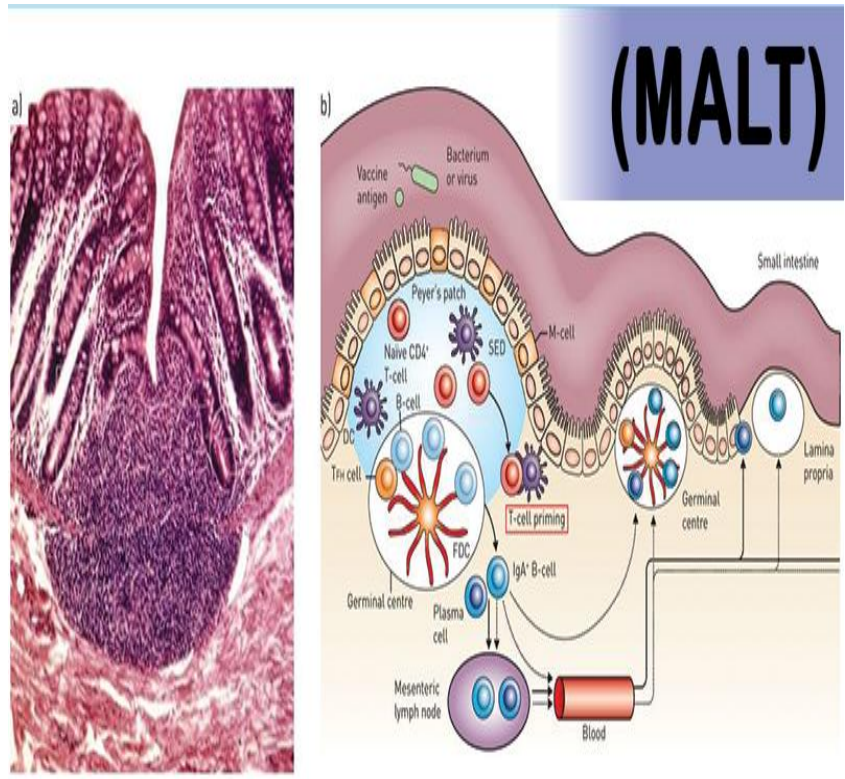
- Bone marrow is probably the largest secondary lymphoid tissue in the body.
- During the primary immune response, antibodies are largely produced in the spleen and Lymph node.
- Towards the end of that response, the memory cells leave the spleen and colonize in bone marrow.
- When a second dose of antigen is given, the bone marrow produces very large quantities of antibodies

- **Lymphoid tissues**

- The [MALT](#) and SALT are situated at the most common points of antigen entry, behind the [mucosal membranes](#) of the respiratory, gastrointestinal, and urogenital tracts, and just below the skin. Large populations of [T and B lymphocytes](#), macrophages, and plasma cells.



**Figure 13.9: Skin-Associated Lymphoid Tissue (SALT)**



The mucosa-associated lymphoid tissues( MALT)and the skin-associated lymphoid tissues(SALT).

## COMPARISON OF PRIMARY AND SECONDARY LYMPHOID ORGANS

<b>Characteristics</b>	<b>Primary Lymphoid organs</b>	<b>Secondary Lymphoid organs</b>
<b>Origin</b>	<u>Ecto-endodermal junction or endoderm</u>	<u>Mesoderm</u>
<b>Time of development</b>	Early in embryonic life	Late in foetal life
<b>Effects of removal</b>	Loss of lymphocytes and immune response	Minimal or no effects
<b>Response to antigen</b>	Not dependent	Fully reactive
<b>Examples</b>	Bone marrow, thymus, bursa, Some peyer's patches	Spleen, lymph nodes, MALT etc.